

REMARKS

Status of the Application

Claims 1-4, 6-11, and 15-27 were pending in the application at the time the Office Action was mailed. Claims 1-4, 6-11, 15-23, 25 and 26 were rejected. Claims 24 and 27 were objected to.

Upon entry of this amendment, claims 1, 2, 4, 9-11, 15, and 17 will have been amended; claims 7, 8, 24, and 27 will have been canceled; and no new claims will have been added. Therefore, claims 1-4, 6, 9-11, 15-23, 25, and 26 will be pending. Entry of this amendment and consideration of these claims is respectfully requested.

Claim Objections

Claims 24 and 27 were objected to for being in improper multiple dependent form. Upon entry of this amendment, claims 24 and 27 will have been canceled.

Rejections Under 35 U.S.C. 112

Claim 4 was rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. According to the examiner:

The specification teaches that the LucCDABE operon contains five genes necessary for self-sustained bioluminescence in bacteria: LuxAB is a luciferase, which catalyzes the light-producing reaction; LuxCE is a multi-component enzyme that converts myristic acid to a fatty aldehyde substrate for the light-producing reaction; and LuxD is a transferase that assists LuxCE (e.g., paragraph bridging pages 5-6). The specification

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teaches nucleic acid constructs comprising *luxA* and *luxB* genes in addition to *luxC*, *luxD*, and *luxE* genes (e.g., page 16, lines 22-27). Claim 4 reads on embodiments where the nucleic acid construct comprises *luxA*, *luxC*, *luxD*, and *luxE* genes, or a construct comprising *luxB*, *luxC*, *luxD*, and *luxE* genes. These combinations are not supported by the specification, claims or drawings as originally filed in that the specification teaches that both *luxA* and *luxB* are required in addition to the *luxC*, *luxD* and *luxE* genes for all proteins necessary for production of bioluminescence without addition of an exogenous substrate. The response does not point to portions of the specification, claims or drawings as originally filed as support for the amendment of claim 4. Therefore, claim 4 represents a departure from the specification, claims and drawings as originally filed.

To address this rejection, upon entry of this amendment, claim 4 will have been amended to depend from claim 1, rather than claim 3. Thus, claim 4 would no longer include the limitation of a purified nucleic acid "wherein said gene cassette encodes all proteins necessary for production of bioluminescence without addition of an exogenous substrate."

Applicants wish to emphasize, however, that the specification does indeed provide support for purified nucleic acids containing either modified *luxA* or modified *luxB*. See, for example, lines 8-9 of page 14 which state "[f]or production of *luxA* variants, *luxBaav*, and wild-type *luxB*, the genes were independently amplified and cloned."

Claims 1-4, 6-11, 15-23, and 25-26 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Upon entry of this amendment, claims 7 and 8 will have been canceled. Although Applicants neither agree nor acquiesce in the rejections set forth in the Office Action, for the sole purpose of

expediting prosecution of the application, upon entry of this amendment, claim 1 will have been amended to recite "at least one modified protein selected from the group consisting of: a modified LuxA comprising an amino acid sequence in its carboxy terminus that specifically binds to a tail-specific protease, and a modified LuxB comprising an amino acid sequence in its carboxy terminus that specifically binds to a protein associated with a ubiquitin-proteasome pathway...wherein the half-life of the modified LuxA protein when expressed in a bacterial cell is shorter than the half-life of the wild-type form of the LuxA protein when expressed in the bacterial cell, and wherein the half-life of the modified LuxB protein when expressed in a yeast cell is shorter than the half-life of the wild-type form of the LuxB protein when expressed in the yeast cell."

The Office Action alleges that the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." See *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir.1991). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Applicants submit that amended claim 1 is fully enabled by the specification and that one of skill in the art could make and use the invention as claimed without undue experimentation.

The Office Action states that the specification is enabling for a purified nucleic acid construct comprising a gene cassette encoding (1) a modified LuxA comprising a carboxy-terminal sequence selected from the group consisting of SEQ ID NOs: 8, 9 and

10, wherein the half-life of the modified LuxA protein when expressed in an *E. coli* cell is shorter than the half-life of the wild-type form of the protein when expressed in the *E. coli* cell and (2) a modified LuxB comprising the PEST-rich 178 amino acid carboxy-terminal sequence of G1 cyclin Cln2, wherein the half-life of the modified LuxB protein when expressed in a yeast cell is shorter than the half-life of the wild-type form of the protein when expressed in the yeast cell.

While Applicants agree with the Office Action's statement that the specification is enabling for a gene cassette encoding a modified LuxA comprising a carboxy-terminal sequence selected from the group consisting of SEQ ID NOs: 8, 9 and 10, wherein the half-life of the modified LuxA protein when expressed in an *E. coli* cell is shorter than the half-life of the wild-type form of the protein when expressed in the *E. coli* cell, Applicants submit that the specification is enabling for amino acid sequences (e.g., C-terminal tags) in addition to SEQ ID NOs: 8-10 that when placed at the carboxy terminus of a protein (e.g., LuxA), specifically bind to a tail-specific protease in bacterial cells. Of the many C-terminal tags known at the time the application was filed, Applicants experimented with 3 of them: SEQ ID NOs: 8-10. The specification, however, cites several references that describe these and other C-terminal tags. Based on the guidance provided by the specification, the existence of working examples, and the high level of skill in the art, it would not require undue experimentation to construct and use modified LuxA proteins having other C-terminal tags in place of SEQ ID NOs: 8-10 in their carboxy termini.

Similarly, while Applicants agree with the Office Action's statement that the specification is enabling for a gene cassette encoding a modified LuxB comprising the

PEST-rich 178 amino acid carboxy-terminal sequence of G1 cyclin Cln2, wherein the half-life of the modified LuxB protein when expressed in a yeast cell is shorter than the half-life of the wild-type form of the protein when expressed in the yeast cell, Applicants submit that the specification is enabling for amino acid sequences, in addition to the PEST-rich 178 amino acid sequence of G1 cyclin Cln2, that specifically bind to a protein associated with a ubiquitin-proteasome pathway in a yeast cell. In the experiments described in the application, a PEST-rich domain that is recognized by SCF (a component of the ubiquitin-ligase complex) was used.

Accordingly, entry of this amendment and withdrawal of these rejections is respectfully requested.

Conclusion


Applicants believe that entry of this amendment would put the current claims in condition for allowance or in better condition for appeal. Applicants submit that the amendment presented herein would revise the form of the claims, but would not raise additional substantive issues. Support for the amendment to claim 1 can be found at page 10, lines 11-28, page 15, lines 12-15, and page 16, line 30 spanning page 17, line 5 of the application. No new matter would be entered by the amendment. Accordingly, entry of the amendment and reconsideration and allowance of the claims is respectfully requested.

The Commissioner is hereby authorized to charge any underpayment or credit any overpayment of fees under 37 CFR 1.16 or 1.17 as required by this paper to Deposit Account 50-3110.

The examiner is cordially invited to call the undersigned if clarification is needed on any matter within this amendment, or if the examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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